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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,072	10/14/2005	Ralf-Holger Voss	BB-140	1890

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
08/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/529,072	VOSS ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 August 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *5* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1-9,12-19,29 and 30*.
   Claim(s) withdrawn from consideration: *20-23,27 and 28*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Shin-Lin Chen/
Primary Examiner, Art Unit 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that the scope of the claims does not encompass the modification of "any and all domains (i.e., extracellular, transmembrane and intracellular domains) of the TCR-complex" by mutagenesis such that "the functionality and stability of the TCR is maintained". Rather, the claims indicate a "surface" on a first and second chain are mutagenized. The specification defines the term "surface" as the area of a TCR that interacts with a particular area of the second chain of the TCR. Applicants cite reference Garcia and argue that the various "surfaces" that interact with one another was known at the time of the invention and the specification also teaches the amino acid residues suitable for mutagenesis (remarks, p. 2-3). This is not found persuasive because of the reasons of record. Since the "surface" is the area of a TCR that interacts with a particular area of the second chain of the TCR, the "surface" can be anywhere in the first and second chains of the TCR, which includes extracellular, transmembrane and intracellular domains. Although the cited Garcia reference shows the 3D-structure of alpha-chain and beta-chain interaction of the TCR, there appears to be several interacting "surface" between those two chains, for ecample, Firues 2 and 4 of Garcia. Further, Garcia only shows one particular TCR complex. Different TCR complex having different amino acid sequences would have different interacting "surfaces" between the alpha-chain and beta-chain. Although it was known how to make mutated TCRs, how to introduce them into cells and how to test TCR functionality, the state of the art at the time of filing was such that the TCR is the most intricate membrane receptor structures known in the art, wherein any mutation in the TCR-complex would cause unintentional conformational changes rendering the scope of invention as claimed highly unpredictable. It was unpredictable at the time of the invention whether the mutations, including reciprocal exchange, introduced to various TCR domains, including extracellular domain, variable domain, constant domain, connecting peptides, transmembrane domain and intracellular domain, would be able to maintain TCR functionality and stability. Applicants cite reference Ogris and argue that delivering system using nucleic acid condensing agents and targeting agents were known and the strategies existed for reducing non-specific interactions with blood components to enable the circulation of complexed DNA in the bloodstream. The non-viral drug delivery systems can be targeted to specific cells via a variety of targeting agetns. Therefore, no undue experimentation is required to direct nucleic acids to T cells in vivo (remarks, p. 4). This is not found persuasive because of the reasons of record. The state of the art of gene therapy in vivo was unpredictable at the time of the invention. One of the greatest challenges facing gene therapy is the efficient transfer and stable expression of transgene in appropriate tissues. The claims encompass using any vector, including viral vector, plasmid, liposome etc., to deliver the claimed DNA molecule to a subject in vivo via various administration routes such that the heterodimeric specific wild type or chimeric T-cell receptor (TCR) protein is expressed and presented by a T cell in vivo. The claims does NOT recite a particular nucleic acid condensing agent or a particular targeting agent. The specification fails to provide enabling disclosure for the full scope of the claimed invention. Therefore, the claims remain rejected for the reasons of record.